TITLE: Preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists

INVENTOR(S): Neustadt, Bernard R.; Lindo, Neil A.; Greenlee, William J.; Tulshian, Deen; Silverman, Lisa S.; Xia, Yan; Boyle, Craig D.; Chackalamannil, Samuel

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

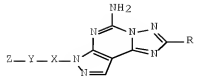
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2001092264	A1	20011206	WO 2001-US16954	20010524	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2410237	A1	20011206	CA 2001-2410237	20010524	<--
CA 2410237	C	20080108			
US 2002099061	A1	20020725	US 2001-865071	20010524	<--
US 6630475	B2	20031007			
EP 1283839	A1	20030219	EP 2001-945991	20010524	<--
EP 1283839	B1	20050420			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
CN 1451007	A	20031022	CN 2001-813449	20010524	<--
JP 2003535094	T	20031125	JP 2002-500877	20010524	<--
BR 2001011015	A	20050111	BR 2001-11015	20010524	<--
AT 293627	T	20050515	AT 2001-945991	20010524	<--
ES 2237576	T3	20050801	ES 2001-945991	20010524	<--
NZ 522326	A	20060331	NZ 2001-522326	20010524	<--
CN 1800186	A	20060712	CN 2006-10004929	20010524	<--
HU 2006000239	A2	20060728	HU 2006-239	20010524	<--
RU 2315053	C2	20080120	RU 2002-135620	20010524	<--
ZA 2002008898	A	20040301	ZA 2002-8898	20021101	<--
NO 2002005651	A	20030123	NO 2002-5651	20021125	<--
MX 2002PA11625	A	20030327	MX 2002-PA11625	20021125	<--
IN 2002CN01932	A	20050211	IN 2002-CN1932	20021125	<--
HK 1049007	A1	20050916	HK 2003-101315	20030221	<--
US 2004023997	A1	20040205	US 2003-448854	20030530	<--
US 6897216	B2	20050524			
US 2005026932	A1	20050203	US 2004-912834	20040806	<--
US 7067655	B2	20060627			
JP 2006219497	A	20060824	JP 2006-128415	20060502	<--
JP 2007145875	A	20070614	JP 2007-69618	20070316	<--

PRIORITY APPLN. INFO.:			
US 2000-207143P	P	20000526	<--
CN 2001-813449	A3	20010524	<--
JP 2002-500877	A3	20010524	<--
US 2001-865071	A3	20010524	<--
WO 2001-US16954	W	20010524	<--
US 2003-448854	A3	20030530	<--

OTHER SOURCE(S): MARPAT 136:20084

GI

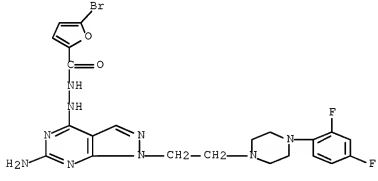


I

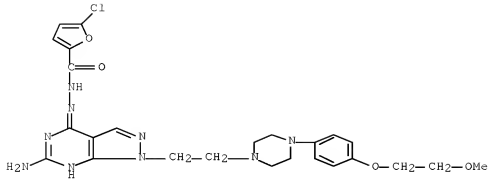
AB The title compds. [I; R = (un)substituted Ph, cycloalkenyl, heteroaryl; X = alkylene, COCH2; Y = O, S, CH2S, (CH2)2NH, etc.; Z = (un)substituted Ph, phenylalkyl heteroaryl, etc.; or Z and Y together are substituted piperidinyl or phenyl], useful in the treatment of Parkinson's disease, alone or in combination with other agents for treating Parkinson's disease, were prepared and formulated. E.g., a multi-step synthesis of I [R = 2-furanyl; X = (CH2)2; ZY = 4-(2,4-difluorophenyl)piperazin-1-yl] was described. Compds. I showed Ki of 0.3-57 nM against A2a receptor binding.

IT 377730-01-3 377730-02-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists)

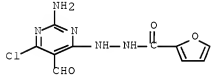
RN 377730-01-3 ZCAPLUS
CN 2-Furancarboxylic acid, 5-bromo-, 2-[6-amino-1-[2-[4-(2,4-difluorophenyl)-1-piperazinyl]ethyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl]hydrazide (CA INDEX NAME)



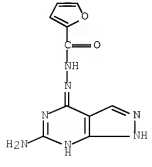
RN 377730-02-4 ZCAPLUS
CN 2-Furancarboxylic acid, 5-chloro-, 2-[6-amino-1-[2-[4-[4-(2-methoxyethoxy)phenyl]-1-piperazinyl]ethyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl]hydrazide (CA INDEX NAME)



IT 377729-80-1P 377729-81-2P 377729-86-7P
377729-93-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-amino-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidines as adenosine A2a receptor antagonists)
RN 377729-80-1 ZCAPLUS
CN 2-Furancarboxylic acid, 2-(2-amino-6-chloro-5-formyl-4-pyrimidinyl)hydrazide (CA INDEX NAME)

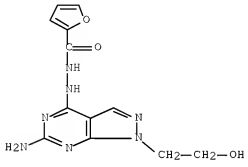


RN 377729-81-2 ZCAPLUS
CN 2-Furancarboxylic acid, 2-(6-amino-1H-pyrazolo[3,4-d]pyrimidin-4-yl)hydrazide (CA INDEX NAME)



RN 377729-86-7 ZCAPLUS
CN 2-Furancarboxylic acid, 2-[6-amino-1-(2-hydroxyethyl)-1H-pyrazolo[3,4-

d]pyrimidin-4-yl]hydrazide (CA INDEX NAME)



RN 377729-93-6 ZCAPLUS
CN 2-Thiophenecarboxylic acid, 2-[6-amino-1-[2-[4-(2,4-difluorophenyl)-1-piperazinyl]ethyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl]hydrazide (CA INDEX NAME)